

FIG. 1A

FIG. 2A

FIG. 2B

FIG. 2C

FIG. 2 D

FIG. 2E

FIG. 2F

MAJORITY	AGCTTCCCCAAGGTGGGGCTTGAGGAGGGCAGGAGGGTACCGTGGAGA	2164
DNAPTAQ
DNAPTFL	A.....	GG.....
DNAPTTH
MAJORITY	CCCTCTTGGCCCCGCTACGTGCCCGACCTAACGCCCGGGTGAAGAGCC	2161
DNAPTAQ	C.....
DNAPTFL	T.....
DNAPTTH	AA..AA..
MAJORITY	GCGCATGGCCTTCAACATGCCGTCCAGGGCACCGGCCGACCTCATGAAG	2170
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	TTCCCCGGCTXAGGAAATGGGGCCAGGATGCTCCXAGGTCCACGAGG	2234
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	CCAAGAGCCGGAGGXGGCTTGGCCAAAGGAGGTCAATGGAGGGGTCTAT	2231
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	CCCC.....	2240
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	AA.....	2234
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2231
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2240
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2304
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2301
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2310
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2374
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2371
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2380
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2444
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2441
DNAPTAQ
DNAPTFL
DNAPTTH
MAJORITY	GG.....	2450

FIG. 2G

MAJORITY CCCCTGGAGGTGGGATGGGGAGACTGGCTCTCCAGGAGTAG

DNAPTAQA.....GA.....	2499
DNAPFLCC.....T.....	2496
DNAPTHGT.....	2505

FIG. 2H

MAJORITY	MXAMILPLFEPKGRVL	LVDGHHLAYRTFFALKGLTTSRGEPVQAVYGFAKSLLKALKEDG	DAVXXVVFDAK
TAD PRO	.RG.H.....	I.....
TFL PRO	V.V.....
TTH PRO	E..	YK.F.....
			69 68 70
MAJORITY	APSFRHEAYAYKAGRAPTPEDFPROLALIKE	LVDLLGLXRLEVPGYEADDVVLATLAKKAKEGYEVRL	
TAG PRO	GG	A.....V.....	S.....
TFL PRO	.	F.....FT	R.....
TTH PRO
			139 138 140
MAJORITY	TADRDLYQLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPSDNLPGVKGIGEKTAXKLLX		
TAG PRO	K.....H.....	D...A....T...E.....	R...E
TFL PRO	E.I.....Y	A.....I.....	QR.IR
TTH PRO	V.V.....H.E	F.V.....	L.K
			209 208 210
MAJORITY	EWGSLENLKNLDRVKP	XXREKIXAHMEDLXLSXXXLSXVRTDOLPLEVDFAXRREPDRREGLRAFLERLEF	
TAG PRO	A.....L..AI.....D..K..WD.AK	K.R.....	
TFL PRO	FQH.Q.....SL.LQ.G.A.A.RK.Q.H	GR.T.NL	
TTH PRO	ENV.K.L.R.LE.R	L.QG	
			278 277 280
MAJORITY	GSLLHEFFGLLEXPKALEEAPWPPPEGA	FVGFFVLSRPEPMMAELLALAARXGRVHRAXDPLXGLRDLKEV	
TAG PRO	S.....	D.....K.....	PE.YKA.....A
TFL PRO	G.A.....L.SF	Q.R.....	G.G.....
TTH PRO	A.AP.....	A.A.....	A.K.....
			348 347 350

FIG. 3A

MAJORITY	RGLLA	KDLAV	ALREG	DLXPGDDPM	LAYL	DPSNTT	PEGVARR	GGW	TEDAGER	ALLSER	LFXNLXX	
TAQ PRO	...	S.	...	G. P.	E.	...	A.	...	WG	418
TFL PRO	...	I.	...	F. E.	A.	...	A.	...	QT. KE	417
TTH PRO	...	S.	...	V.	AH.	...	HR.	...	LK	420
MAJORITY	RLEG	EERLLWLYXEVEKPLSRVL	AHMEATGVRLDVAYL	QALSLEV	AAEIRR	LEEV	FRLAGHP	FNLNSR	D			
TAQ PRO	...	R.	...	R.	...	R.	R.	...	A.	...	A.	488
TFL PRO	...	K.	...	E.	...	R.	EA.	V.	Q.	487
TTH PRO	...	K.	...	H.	L.	490
MAJORITY	QLERV	VLFDELGLPAIGKTEKTGKR	STSAAV	LEALREAHPI	VKEILQY	RELTKLKNTYIDPLP	XLVHP	R	TG			
TAQ PRO	S.	...	D.	I.	558
TFL PRO	DR.	...	A.	...	K.	557
TTH PRO	R...	L...	Q.	H.	V.	S.	560
MAJORITY	RLHTR	FNQTATATGRL	SSSDPNLQNI	PVRTPLGQR	IRRAFVAEEGWXL	VALDYSQIELRV	LAHLS	DENL				
TAQ PRO	I.	...	L.	628
TFL PRO	V.	...	V.	627
TTH PRO	A.	...	A.	630
MAJORITY	IRVFQEGRDI	HTQTASWMFGVPPEAVDPLM	RRAAKTINF	GVLYGM	SAHRLSQ	ELAIPYEAVAFI	ERYFQ					
TAQ PRO	...	E.	...	R.	Q.	...	Q.	698
TFL PRO	...	S.	...	S.	G.	...	S.	697
TTH PRO	...	K.	...	K.	V.	...	V.	700

FIG. 3B

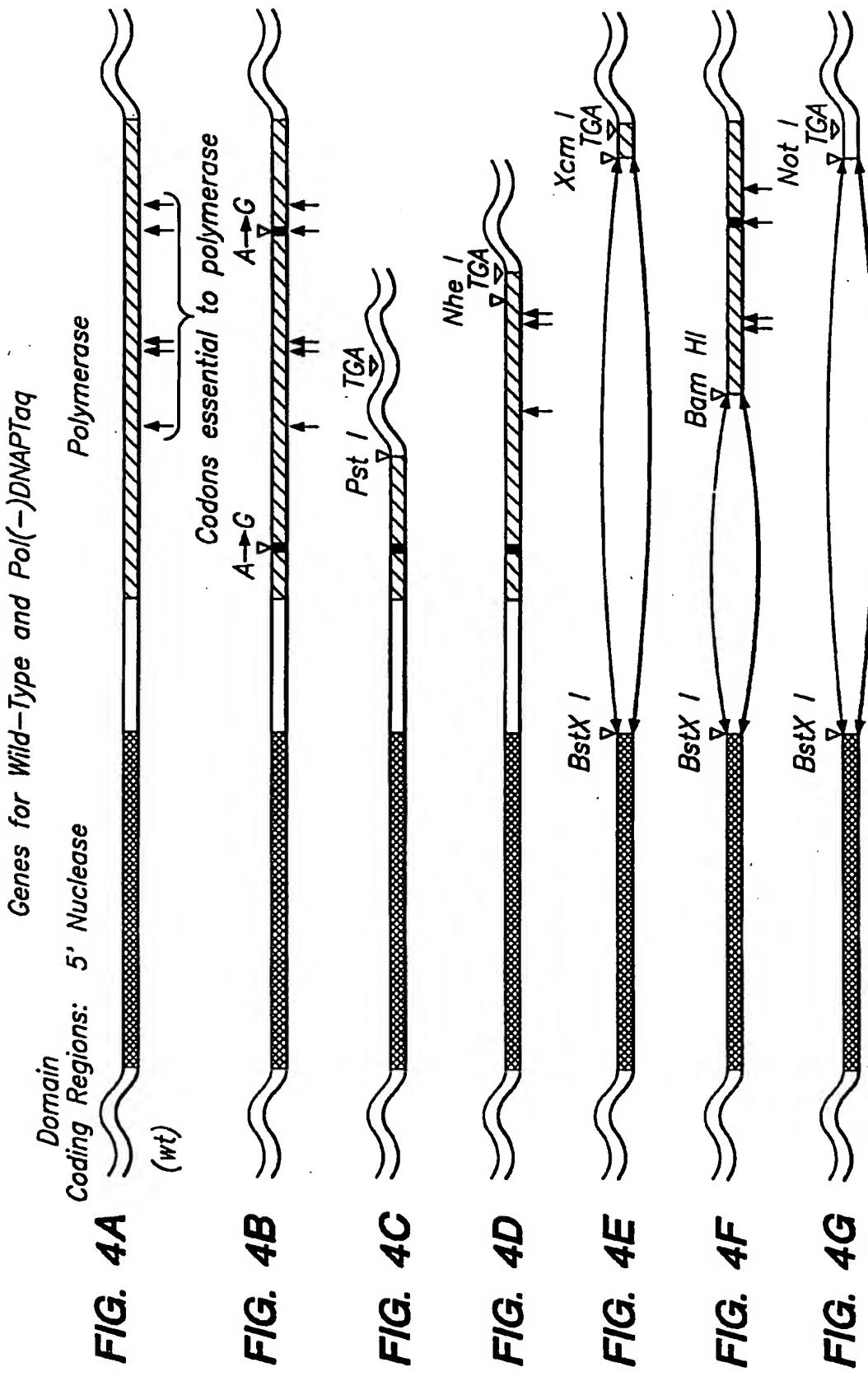
MAJORITY SFPKVRAWIEKTLEEGRRRGYVETLFGRRRYVPDLNARVKSVREAAERMAFNMPVQGTAADLMKLVKL

TAQ	PRO	E	768
TFL	PRO	Y	G	767
TTH	PRO	K	770

MAJORITY FPRIXEMGARMILLQVHDELVLEAPKXRAEXVAALAKEVMEGVYPLAELVEVGXGEDWLSAKEX

TAQ	PRO	E	E	A	R	I	833		
TFL	PRO	Q	L	D	R	W	Q	L	831
TTH	PRO	R	M	835

FIG. 3C



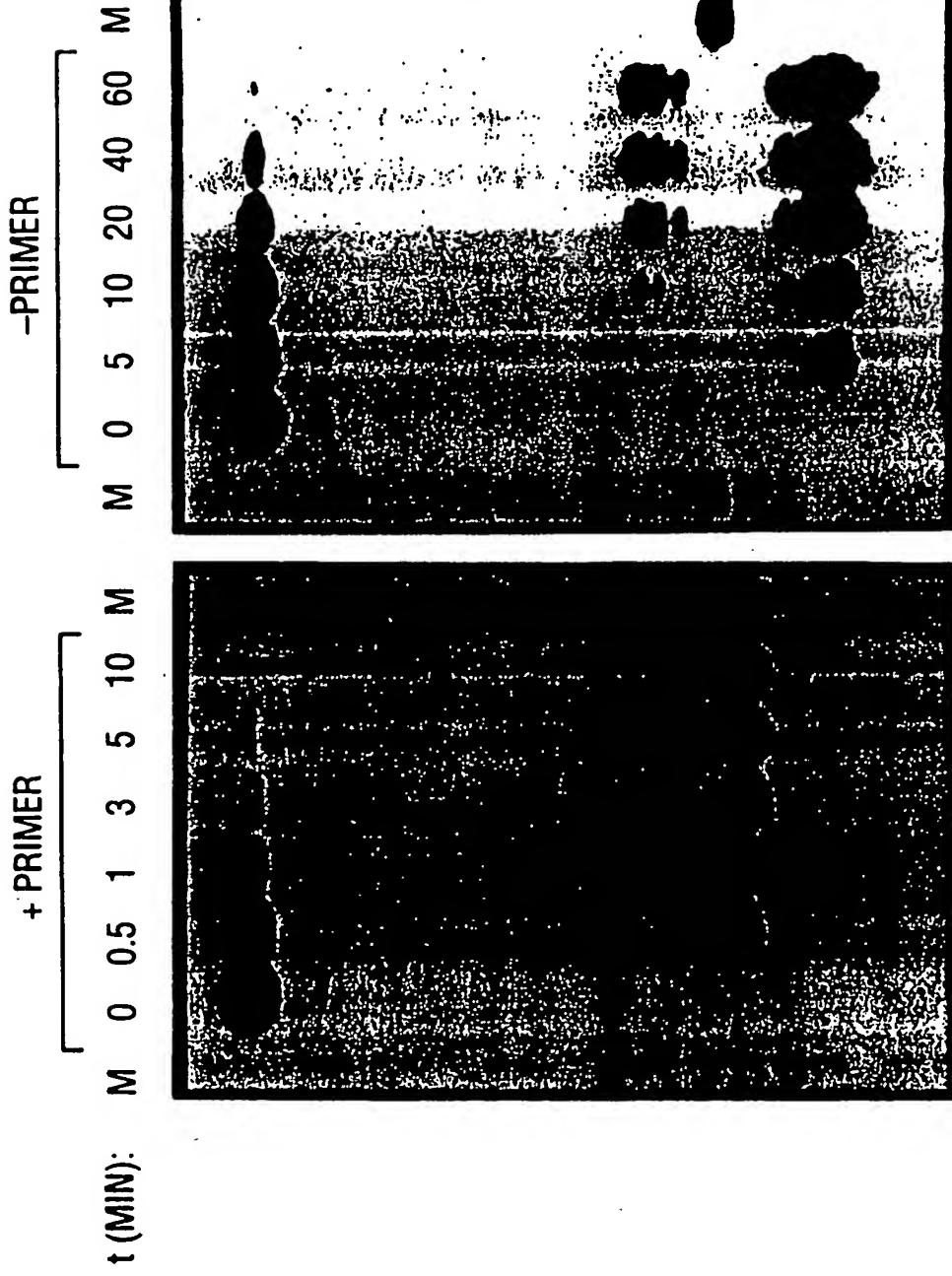


FIG. 10A

FIG. 10B

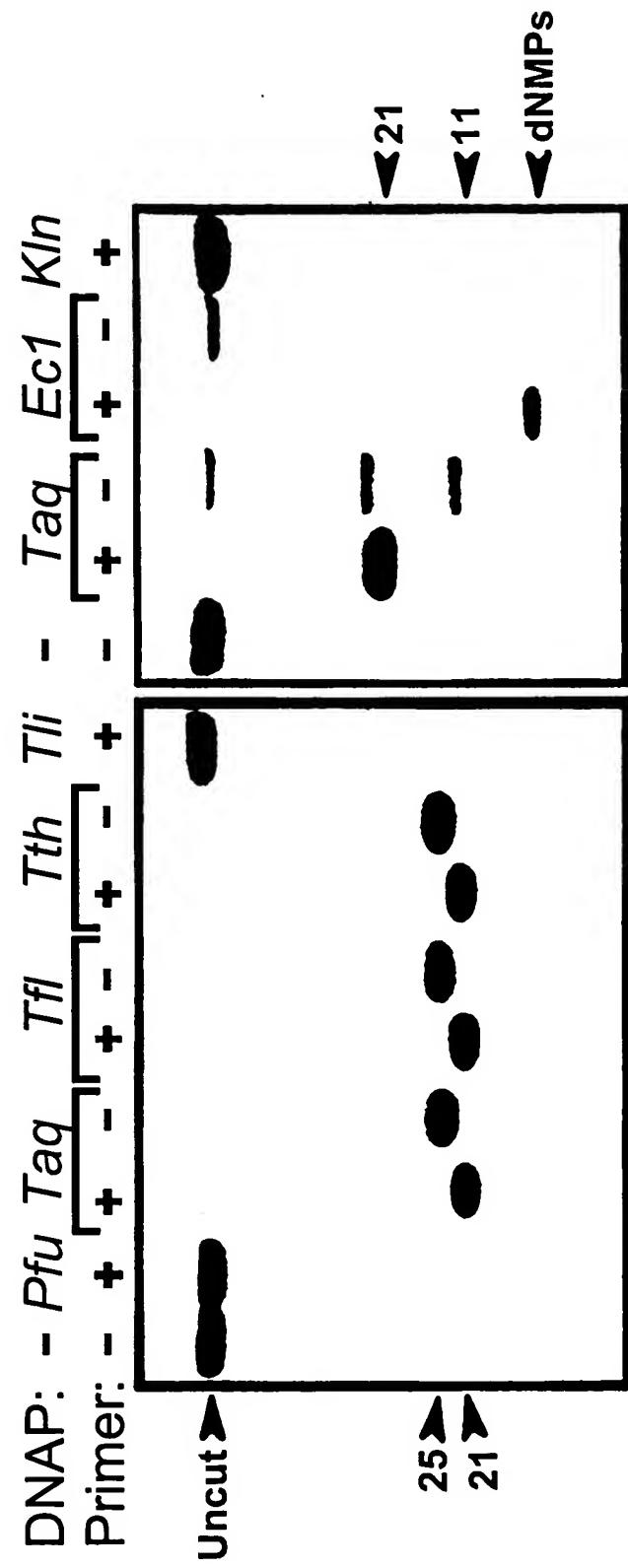


FIG. 11A FIG. 11B

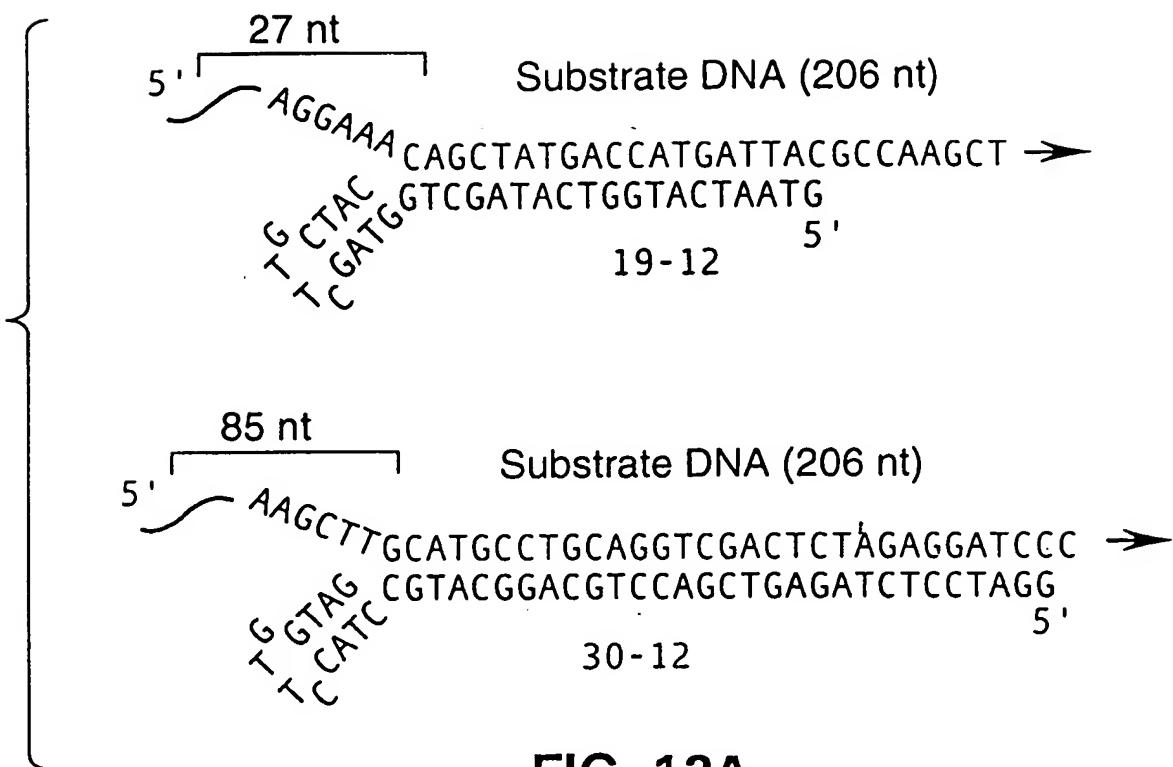


FIG. 12A

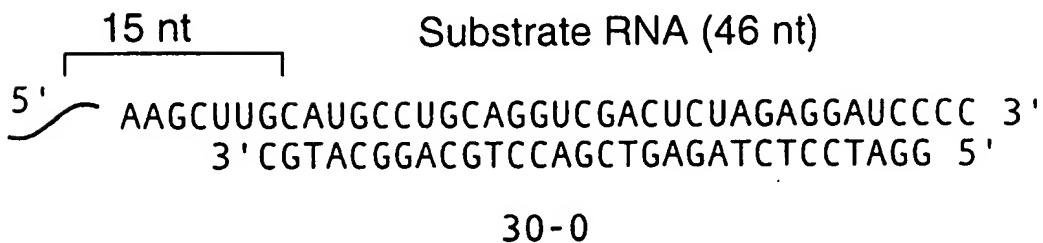


FIG. 13A

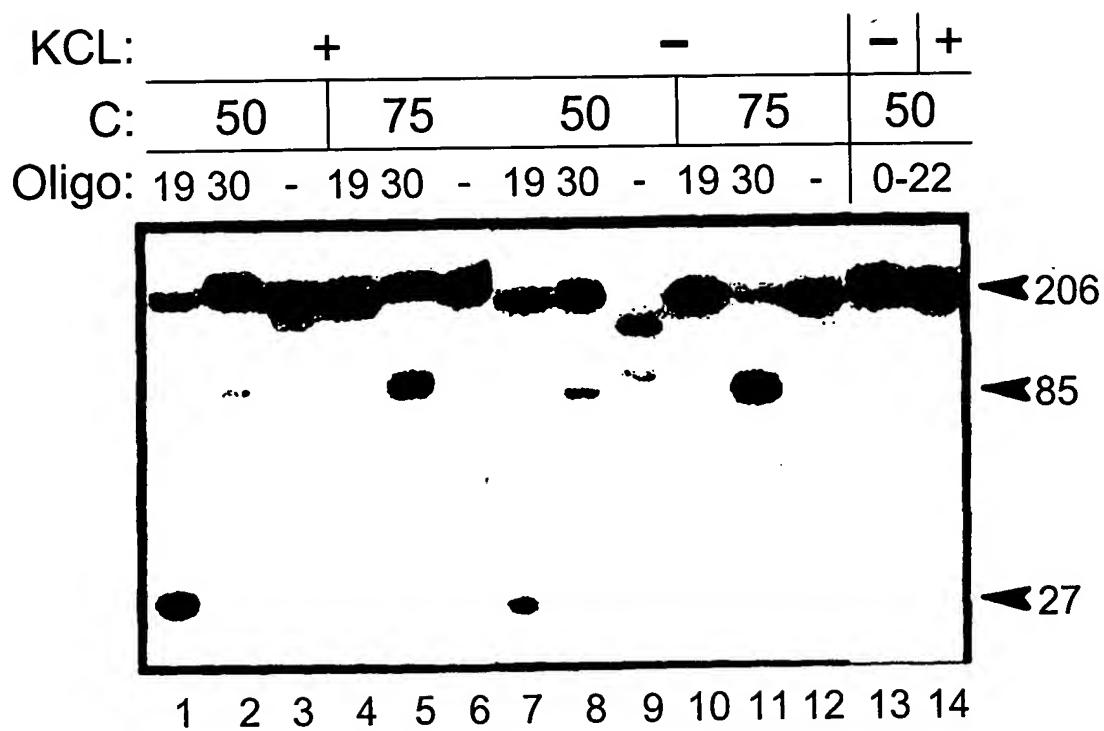


FIG. 12B

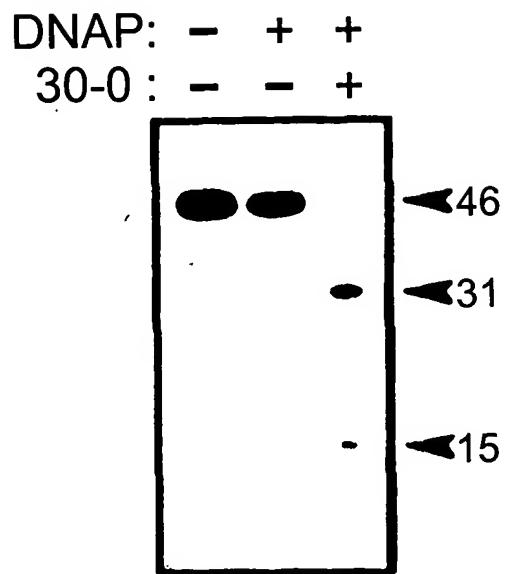


FIG. 13B

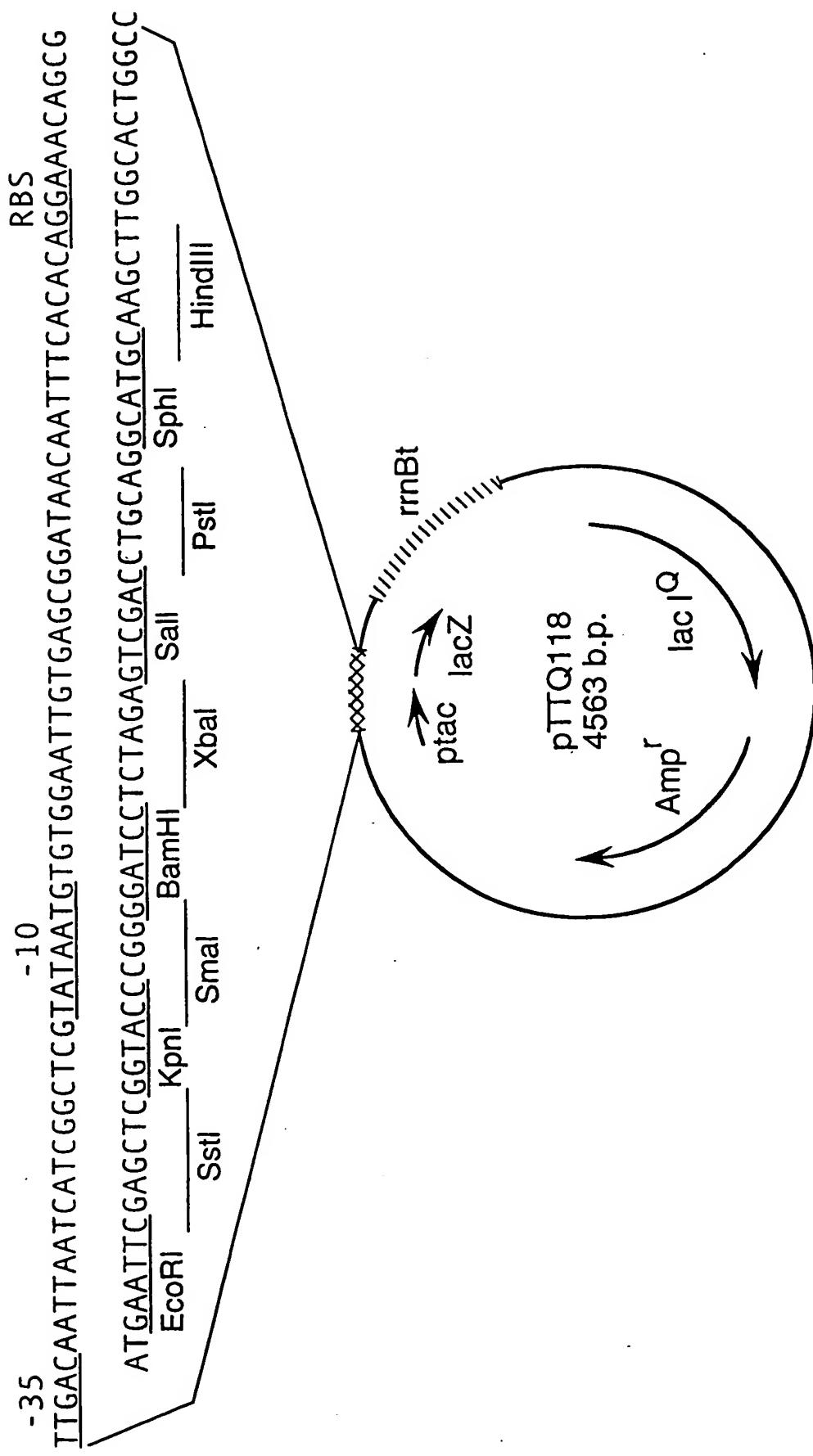
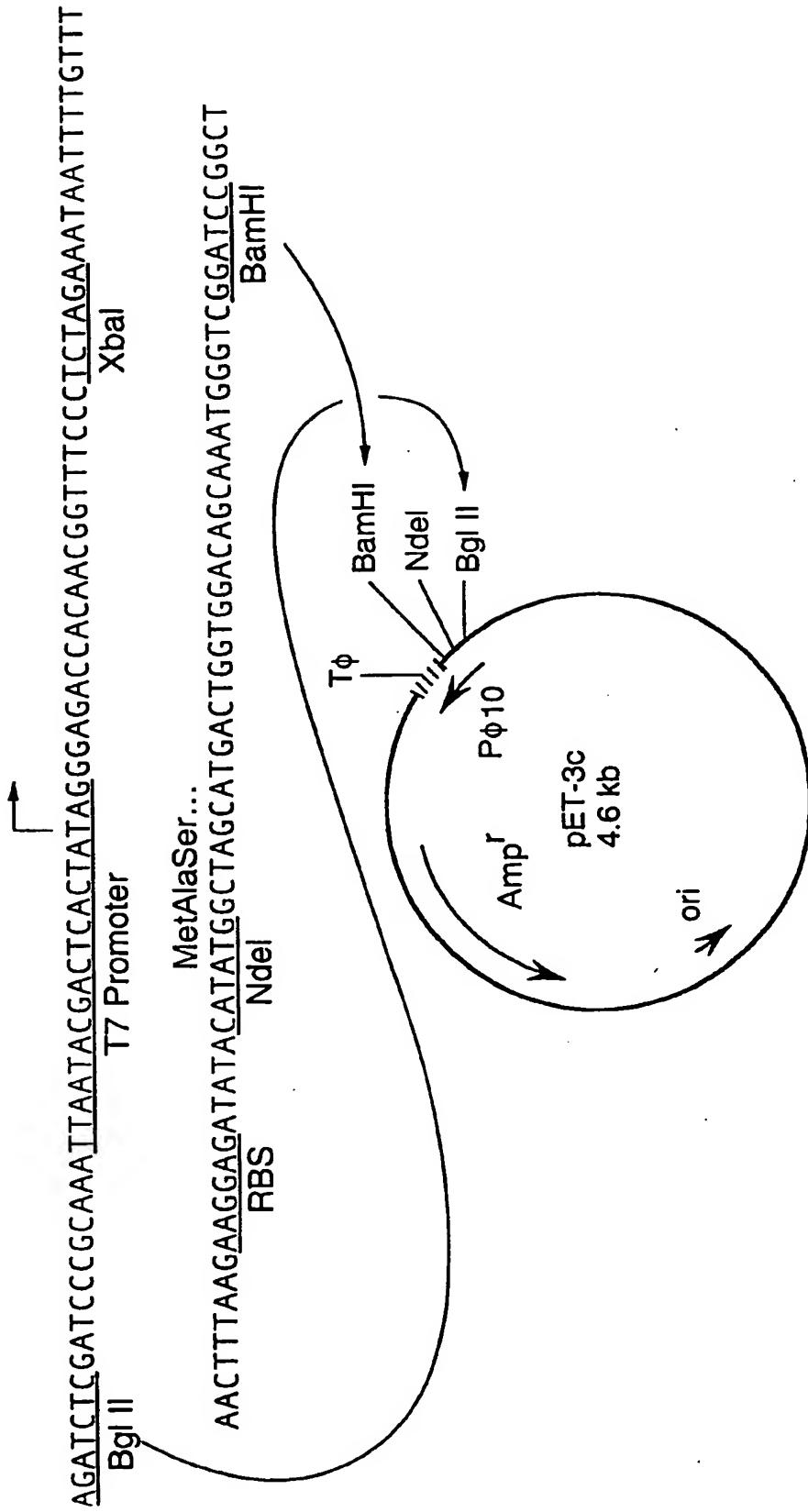


FIG. 14

RBS: Ribosome binding site
 ptac: Synthetic tac promoter
 lac I^Q: Lac repressor gene
 lacZ: Beta-galactosidase alpha fragment
 rrmBt: E. coli rrmB transcription terminator



$P_{\phi}10$: Bacteriophage T7 ϕ 10 promoter RBS: Ribosome binding site
 $T\phi$: T7 ϕ Terminator

FIG. 15

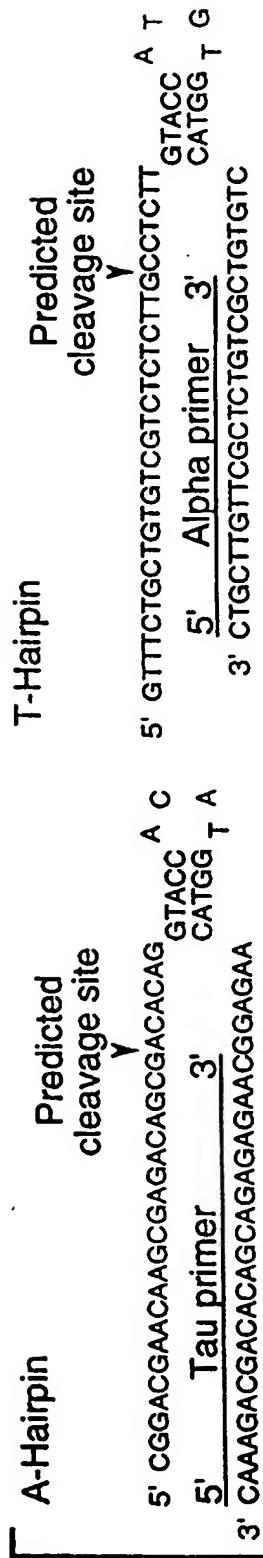


FIG. 20A

Sequence of alpha primer:
5' GACGAAACAAGCCGAGACAGCG 3'

FIG. 20B 5' Tau p
CAAAGACCGACAA
 FIG. 20C

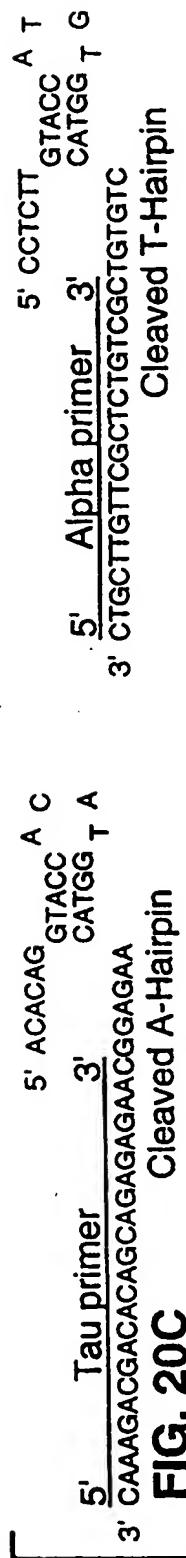
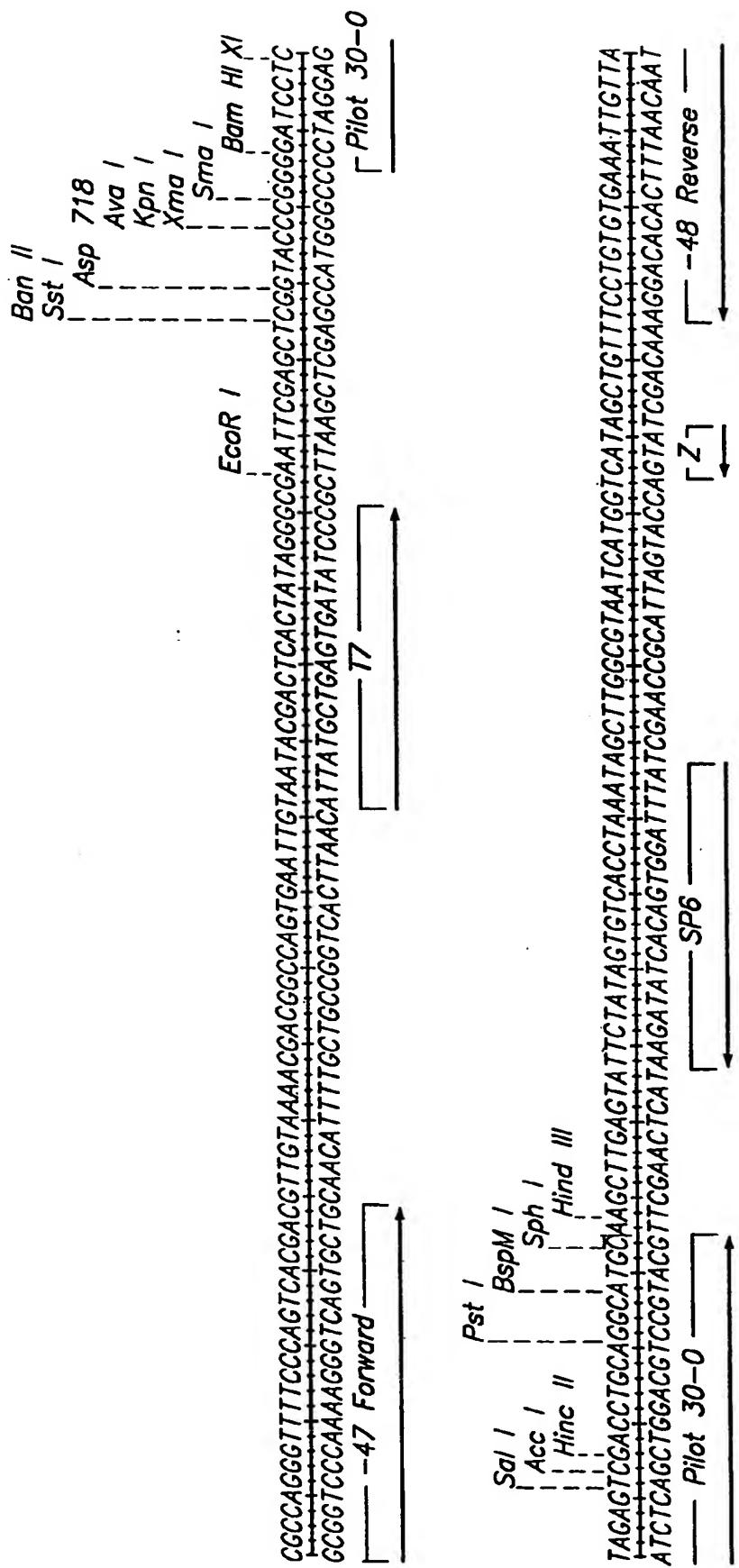


FIG. 20B

FIG. 20D



TCCGCTCACAAATTCCACACAAACATAACGA 228
 ACCCGA β GTTAACGCTGTTGTTGCT 206
 -48 Reverse

FIG. 21

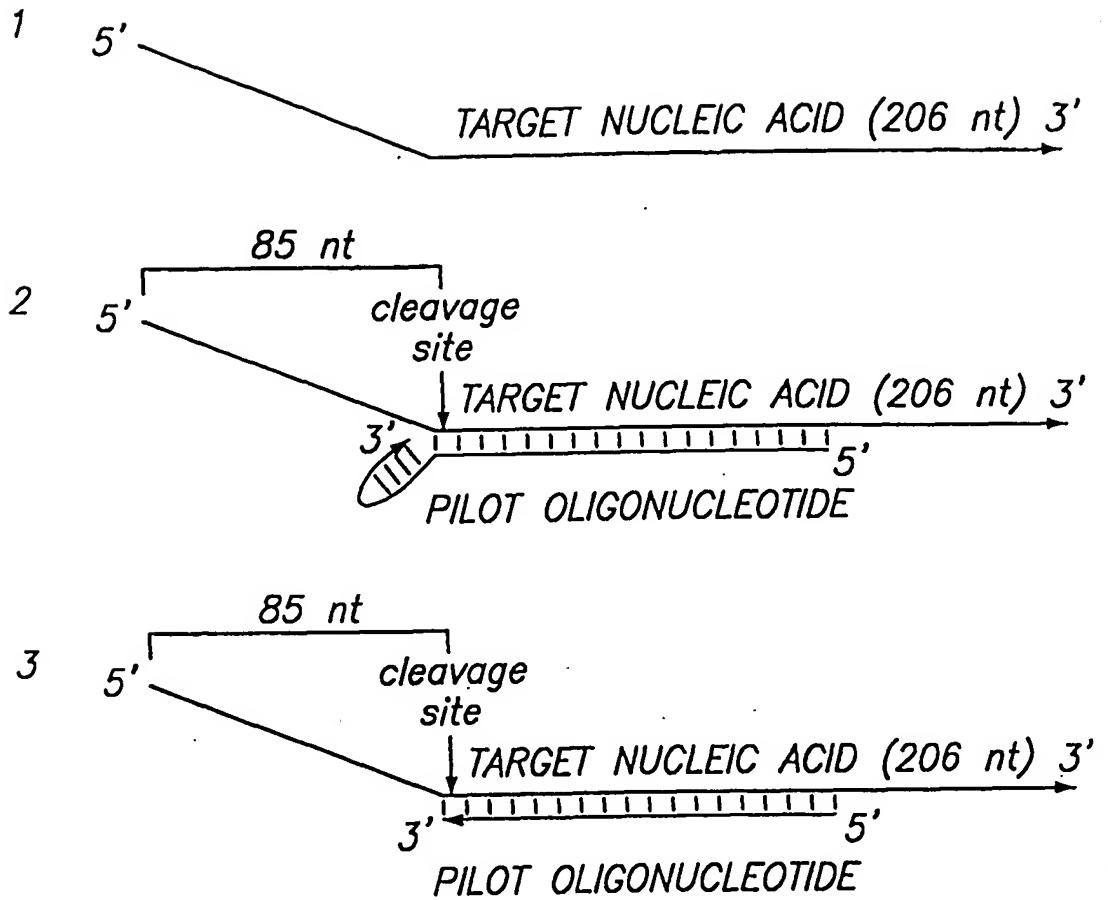


FIG. 22A



FIG. 22B

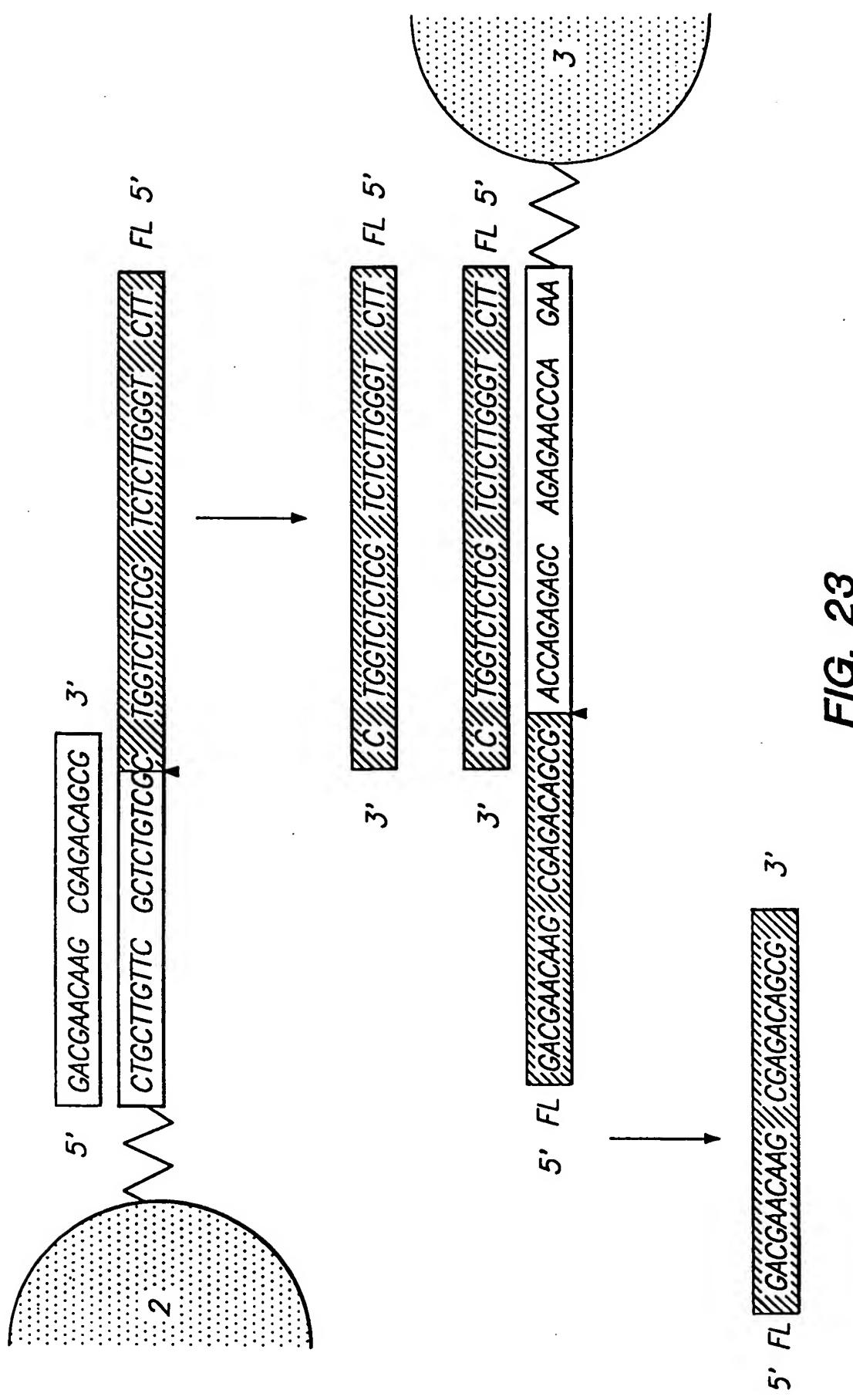


FIG. 23

CDR BEAD	T	T	T	A/T	A	A	A
PILOT	-	-	+	-	+	-	-
CLEAVASE	M	M	-	+	+	+	-

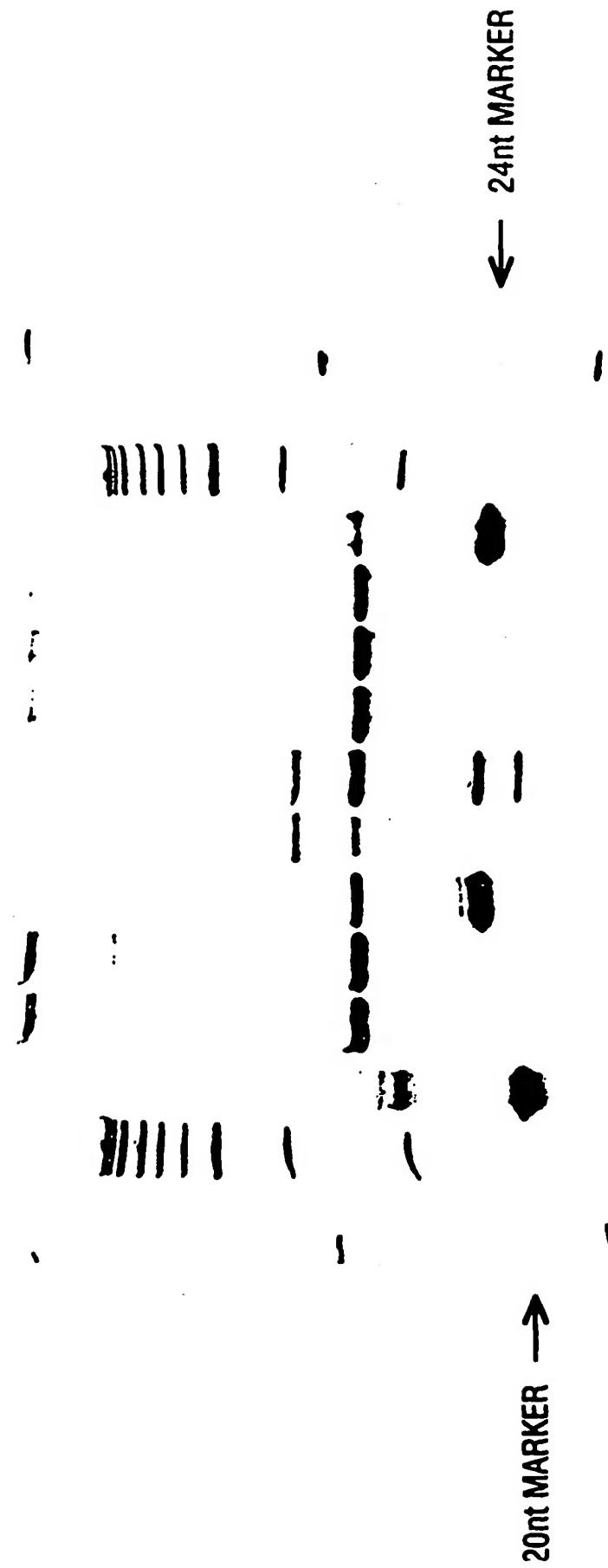


FIG. 24

FIG. 33

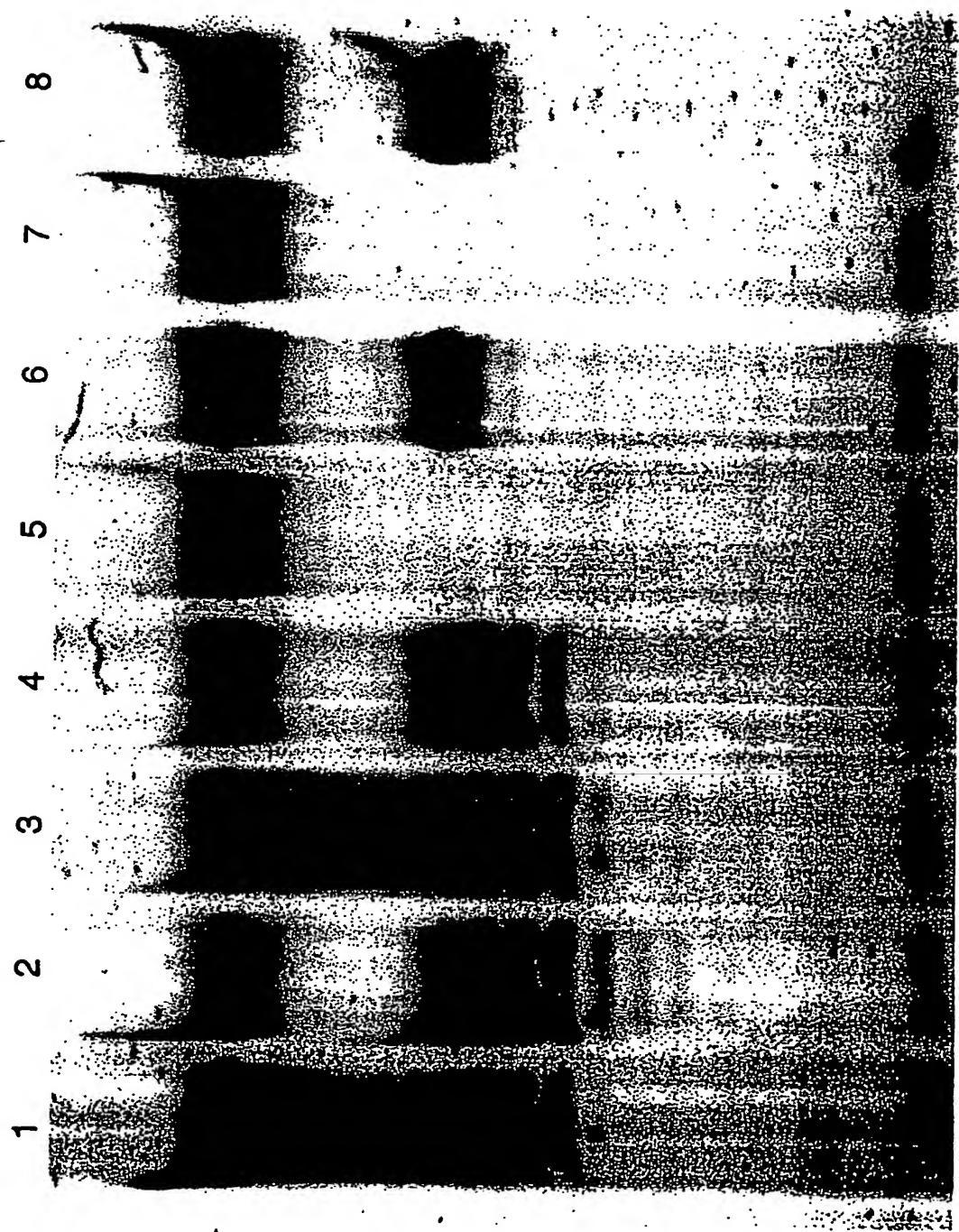
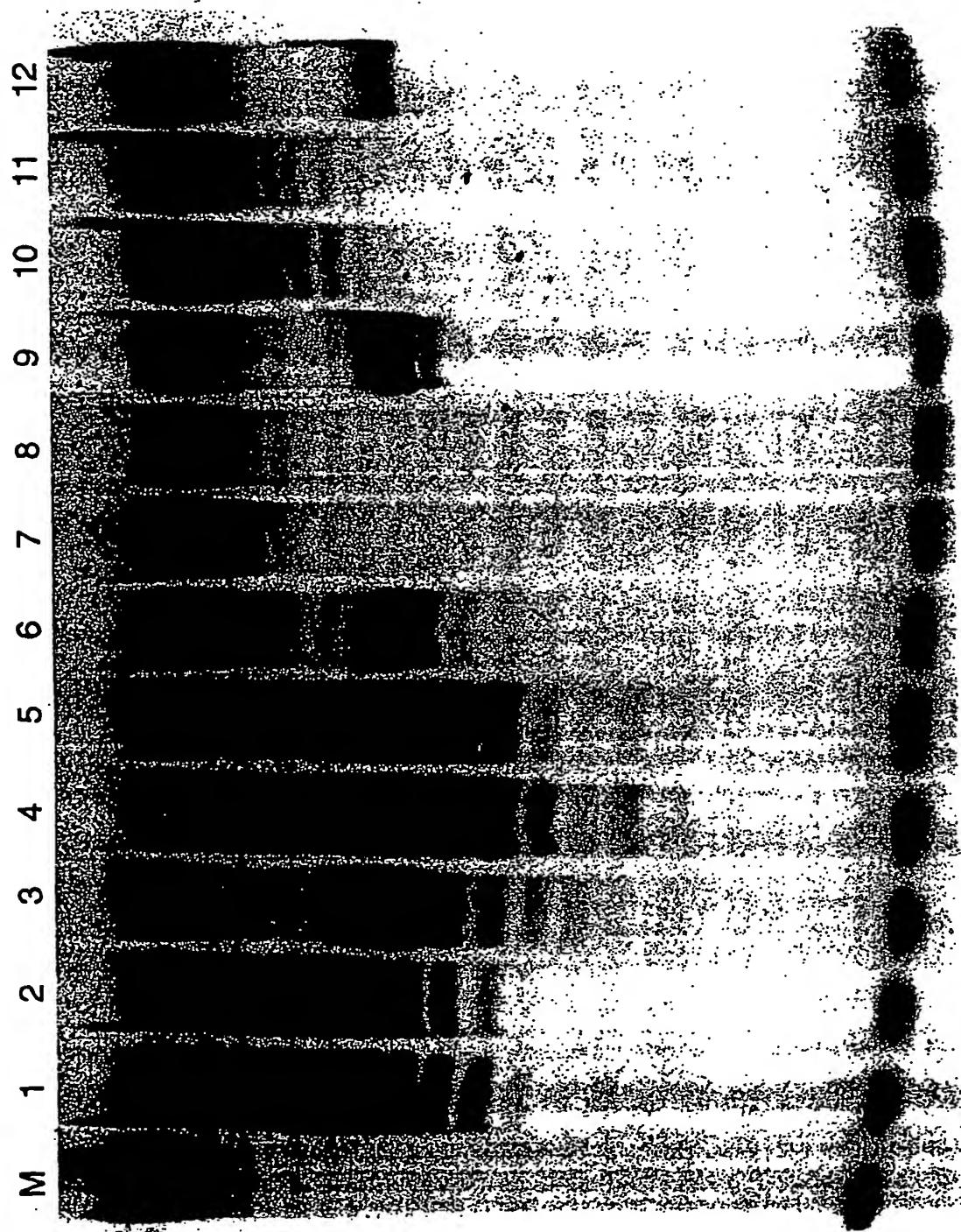


FIG. 34



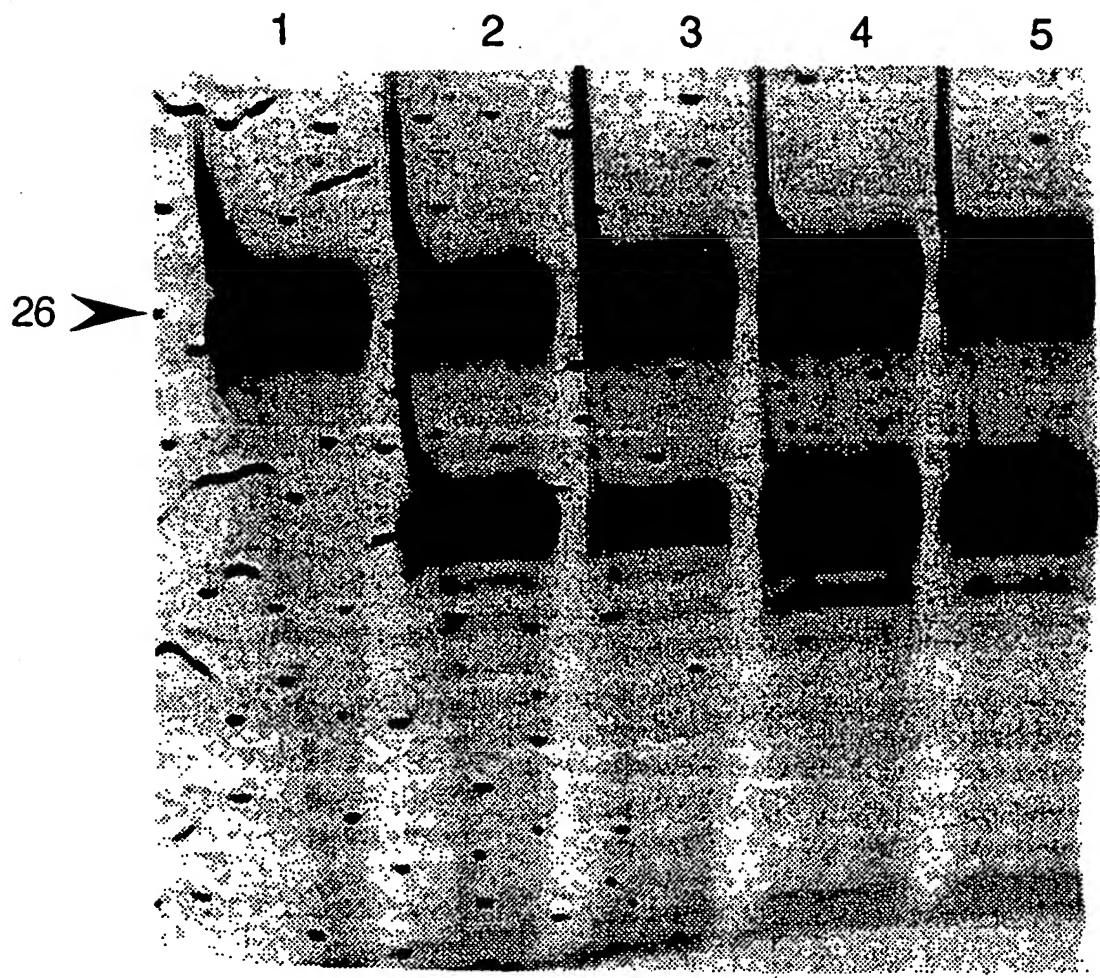


FIG. 35

FIG. 36

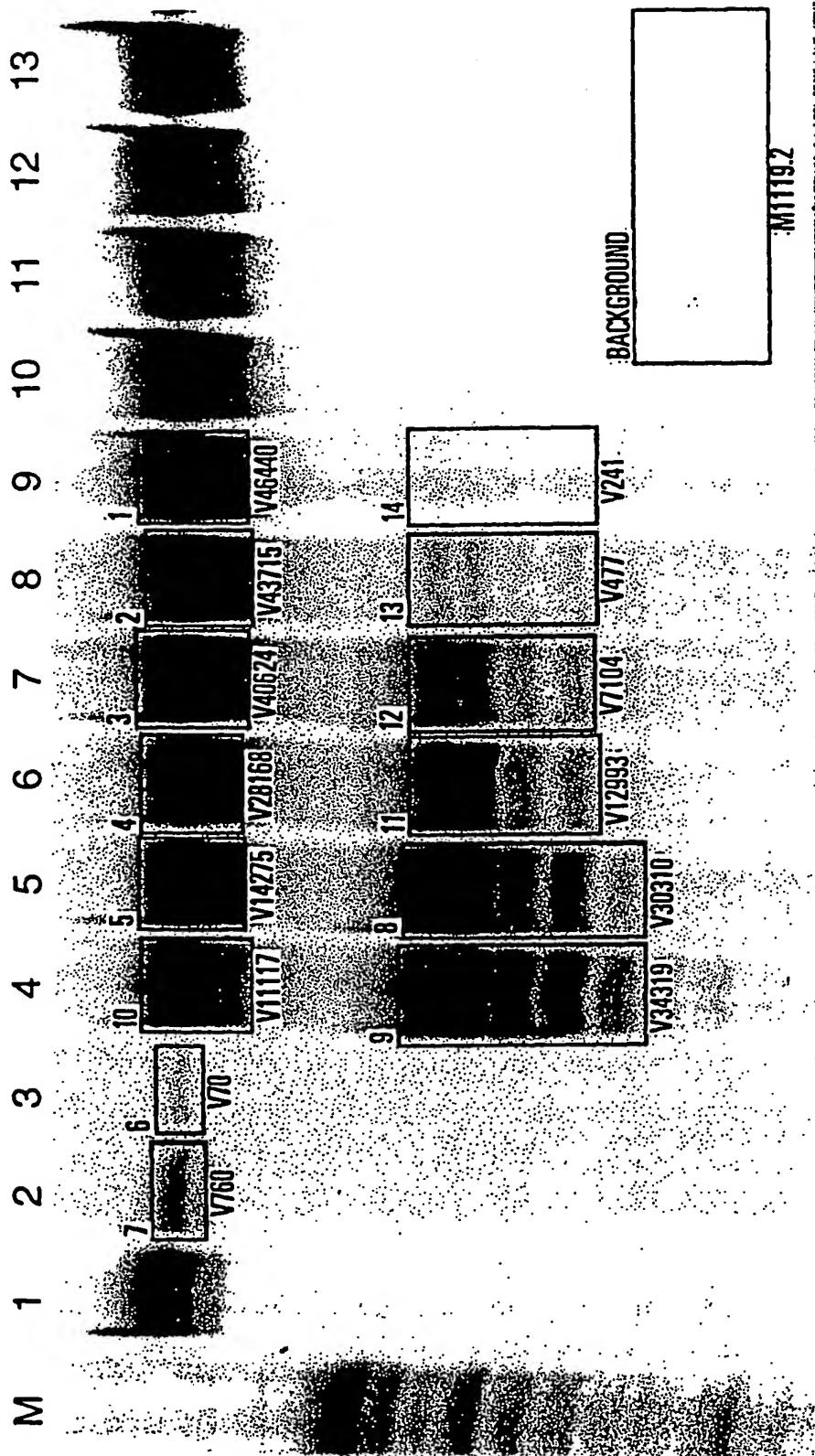


FIG. 53B

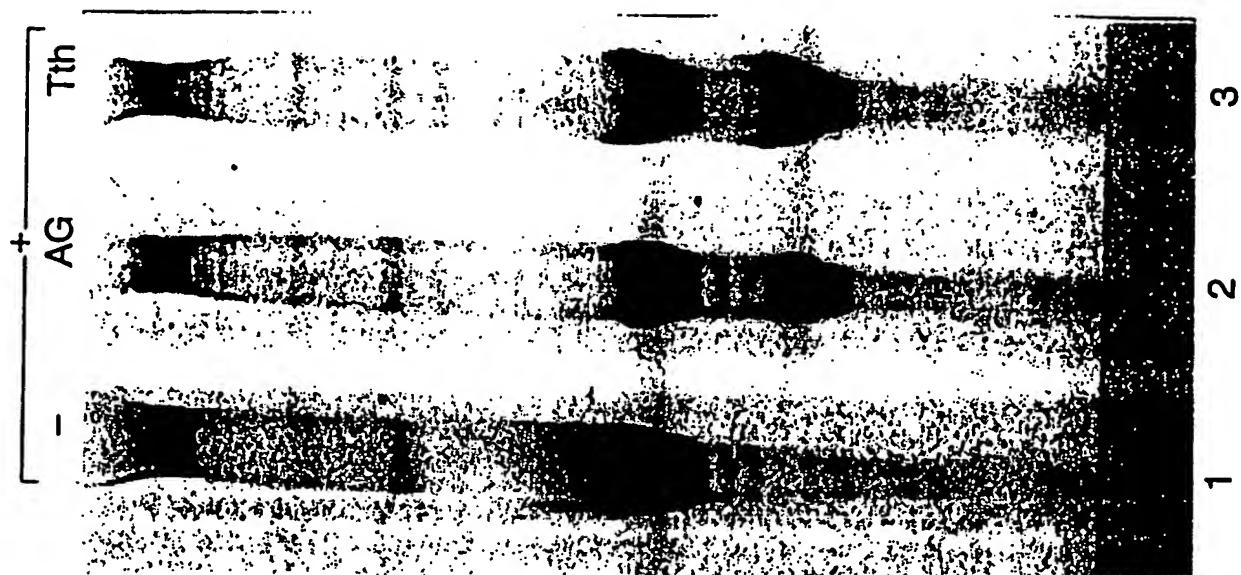


FIG. 53A

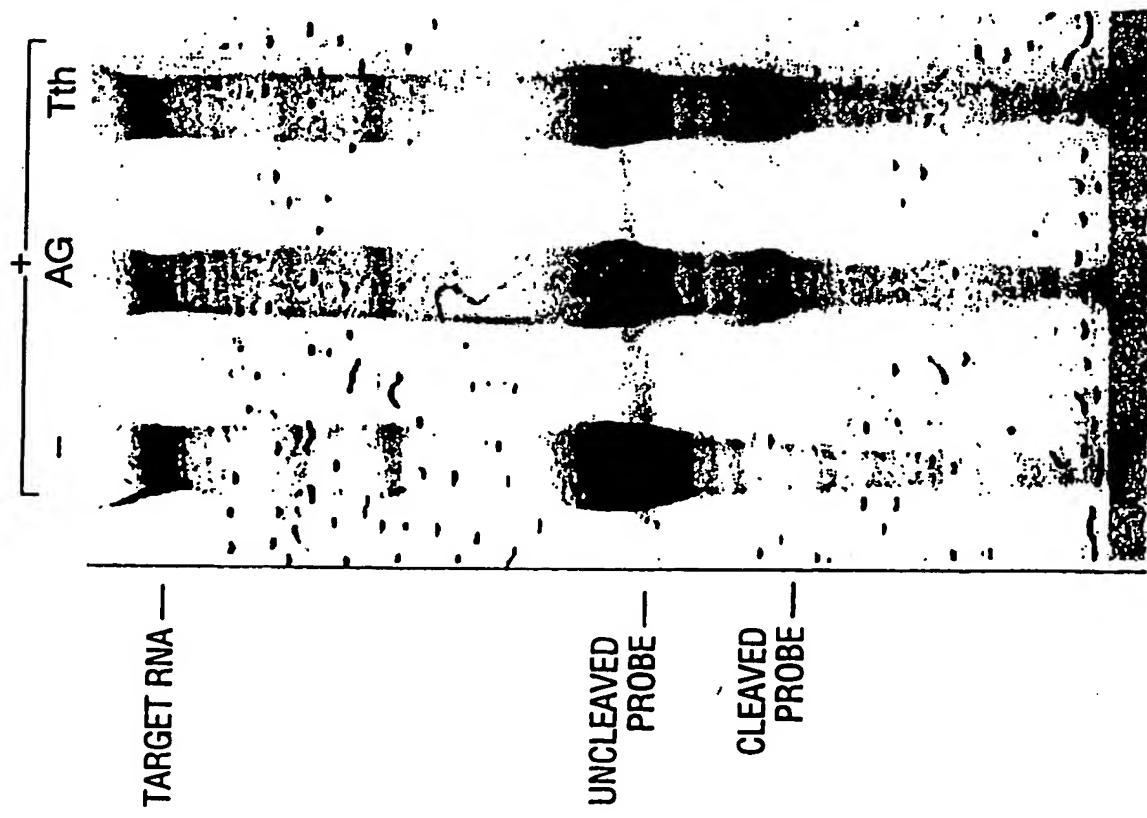
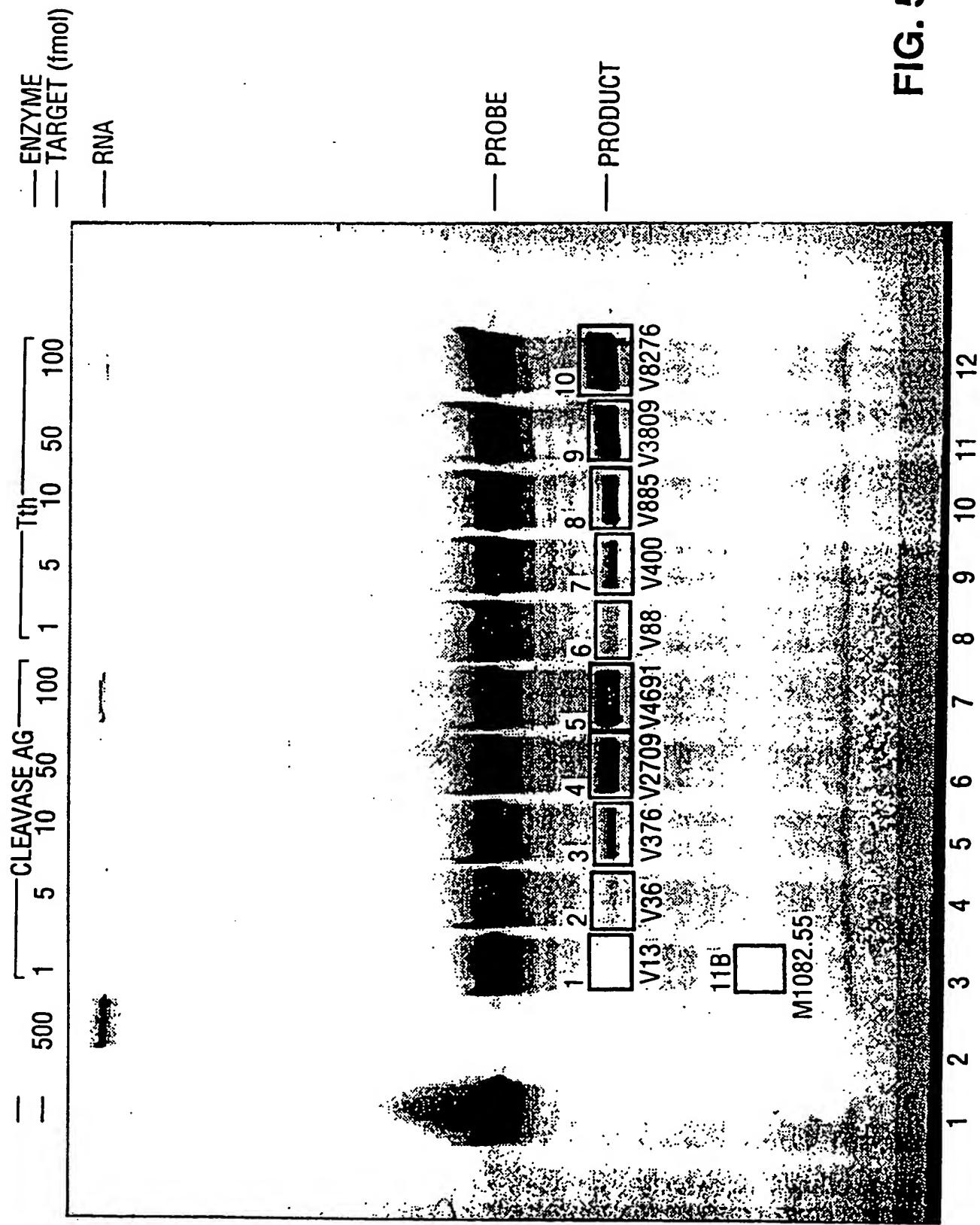


FIG. 54



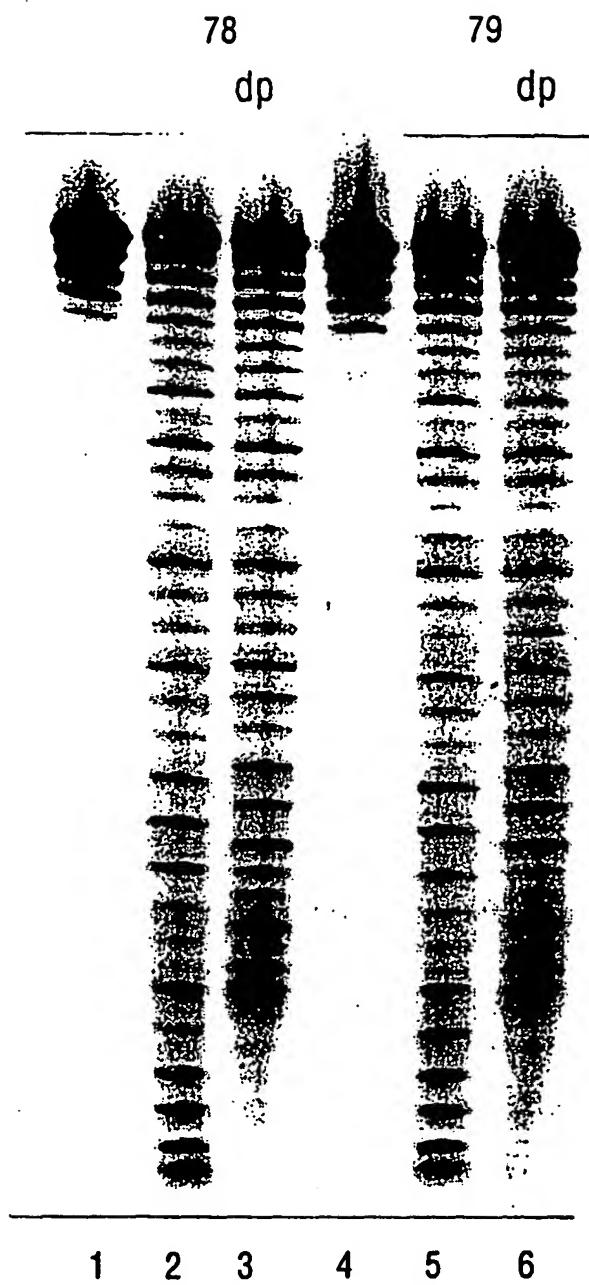


FIG. 55

76

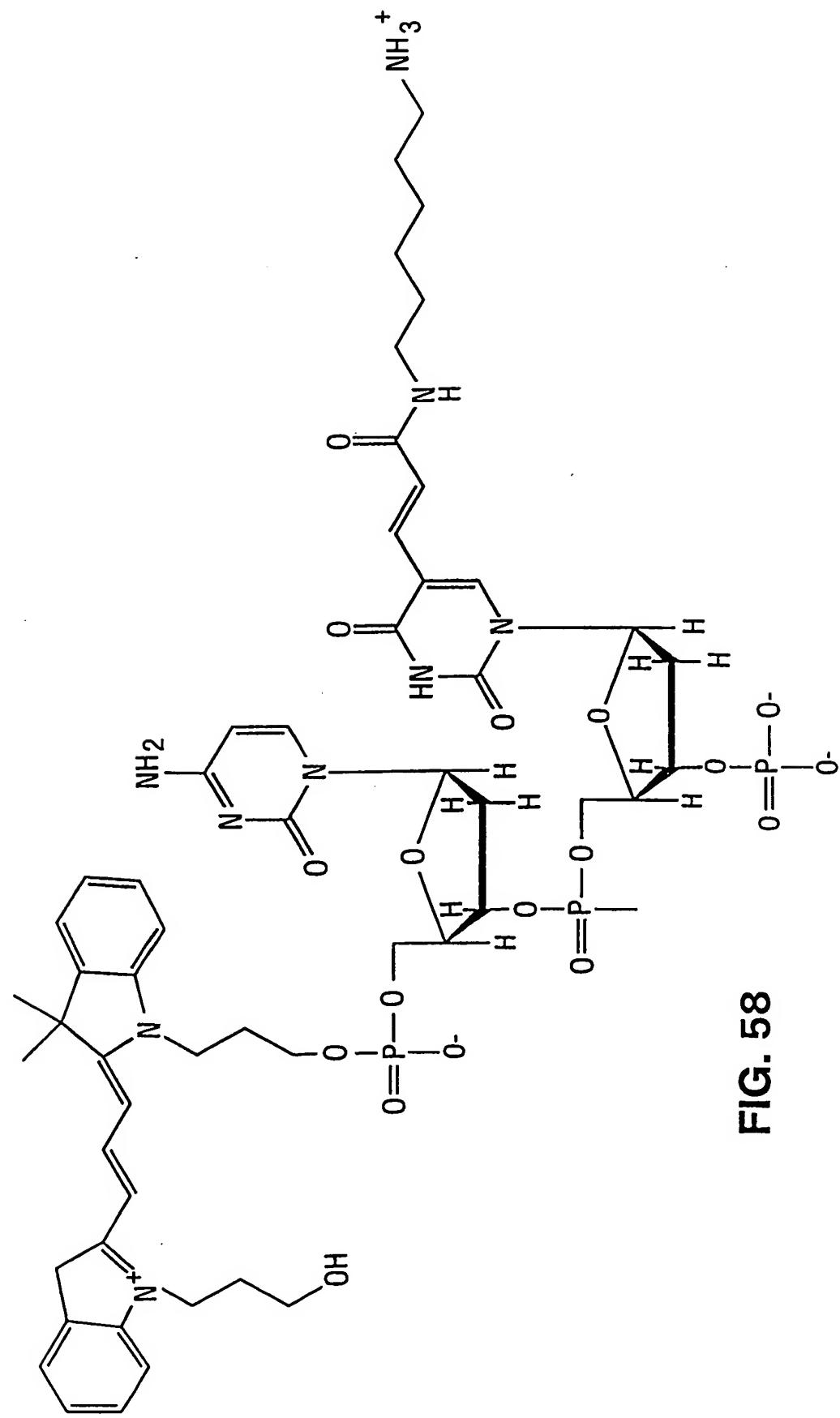


FIG. 58



FIG. 65A

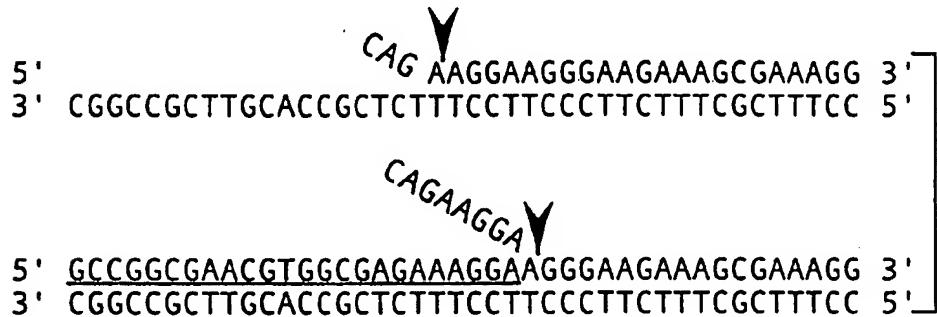


FIG. 65B



FIG. 65C



FIG. 65D

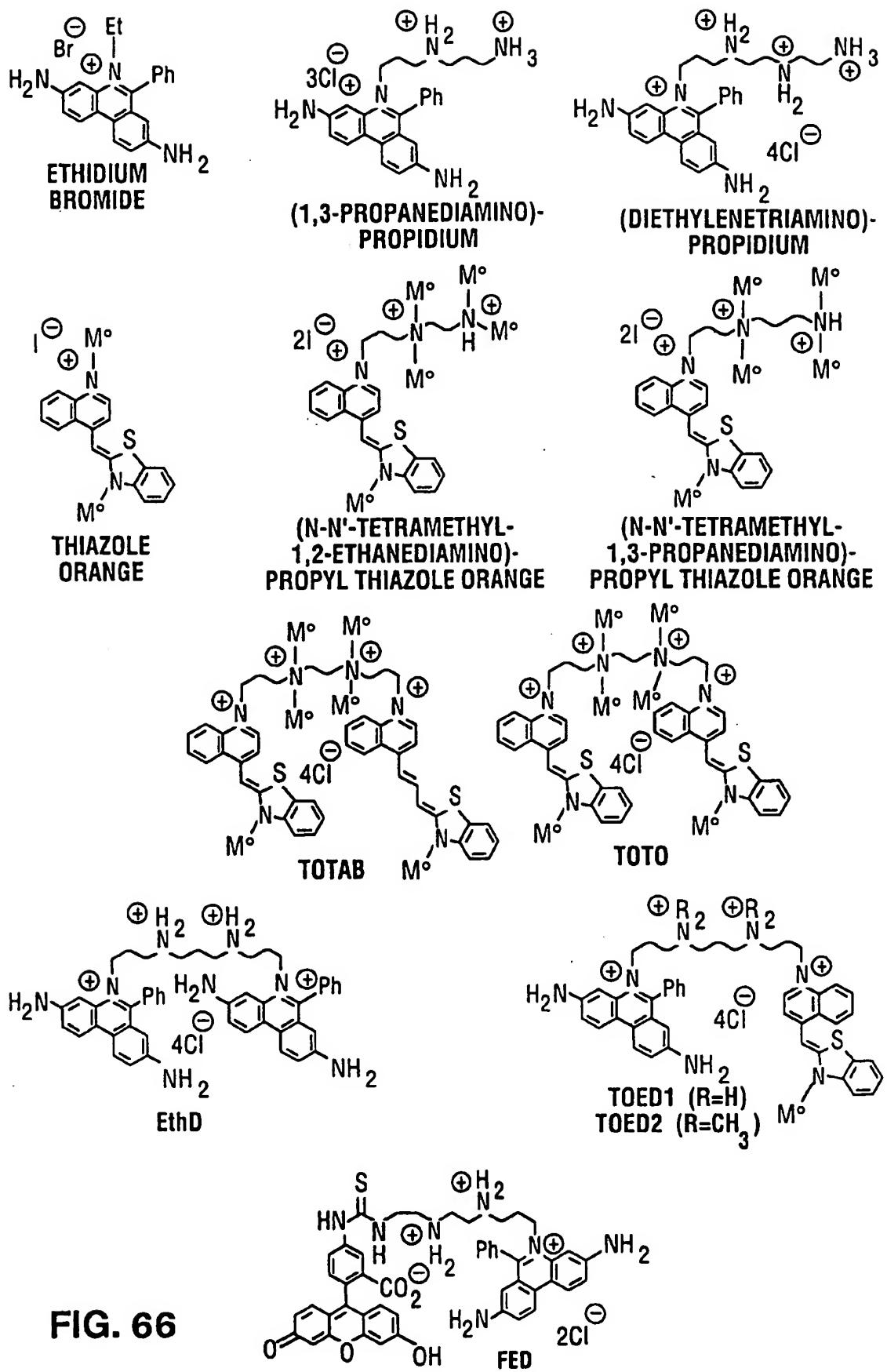


FIG. 66

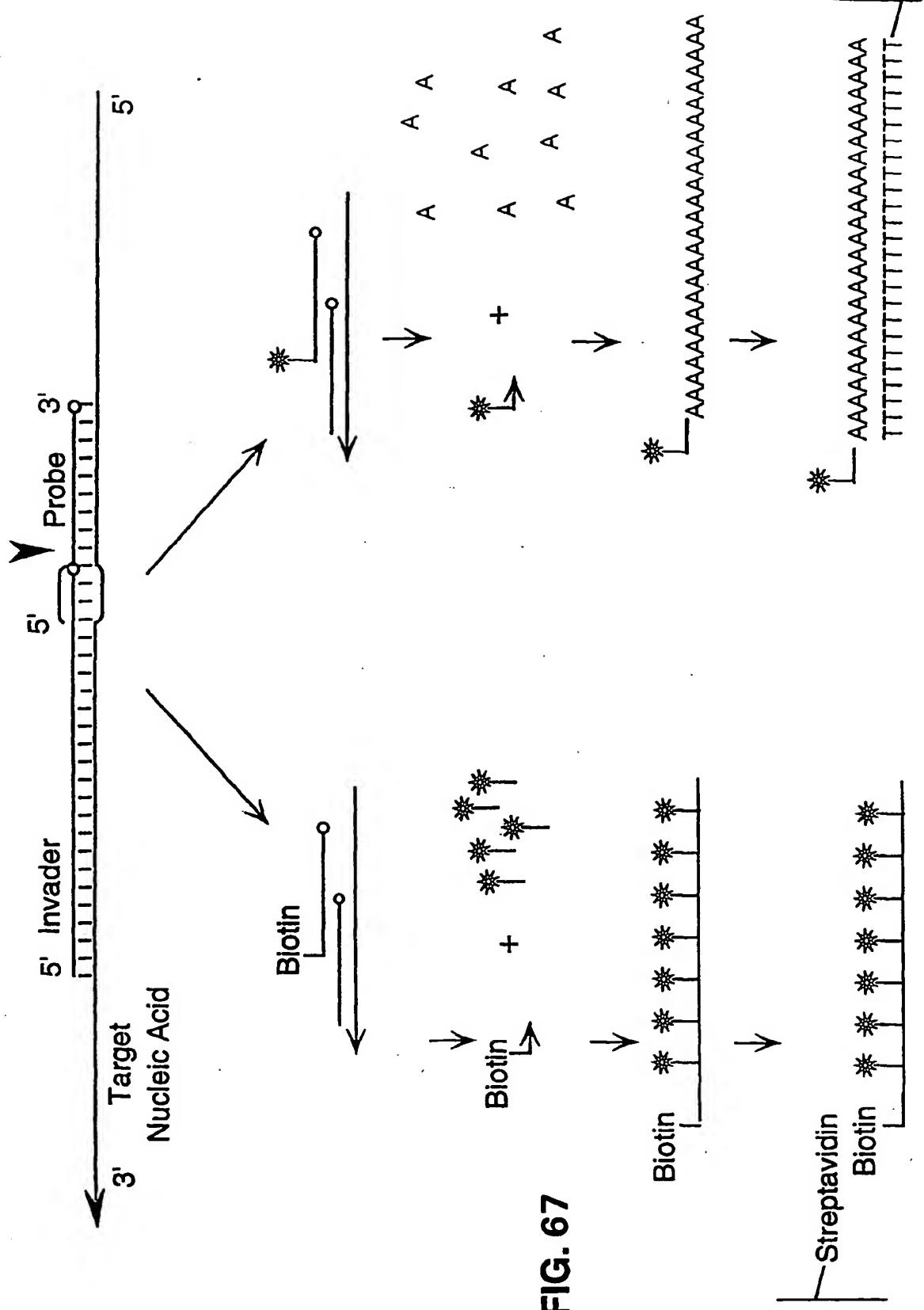


FIG. 67

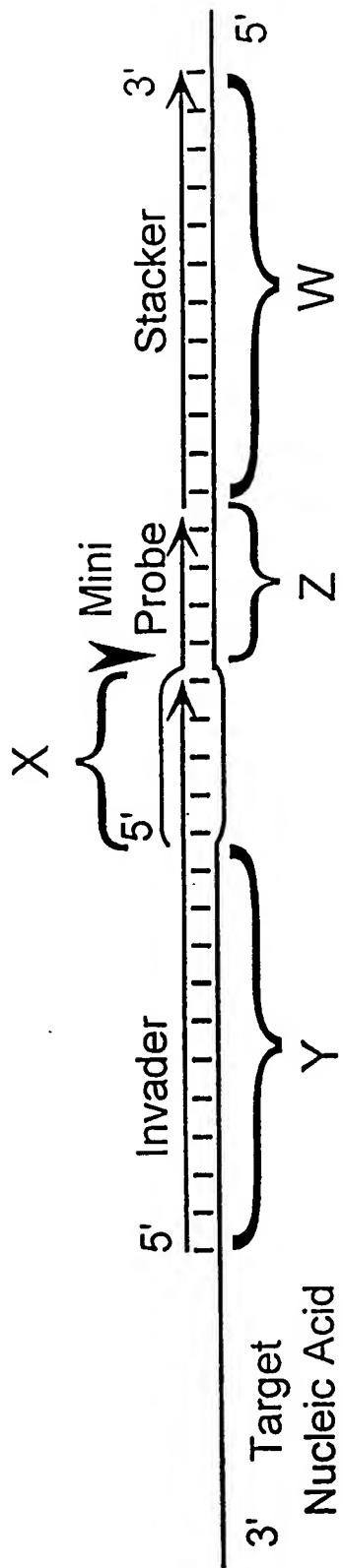


FIG. 68

10	20	30	40	50	60	70				
1 MGVQ----FDFIPK--NIISFEDLKGGKKVAIDGMNALYQFLTSIRLRDGSPLRNRKG EITSAYNGVFY MJAFEN1 . PRO	1 MGVP----IGEIPR--KEIELENLYGKKIAIDALNAIYQFLSTIRQKDGTPMDSKGRITSHLSGLFY PFUFEN1 . PRO	1 MGIQGLAKLIADVAPS AIRENDIKSYFGRKV AI DASMSIYQFLIAVRQ -GGDVLQNEEGETTSHLMGMFY HUMFEN1 . PRO	1 MGIHGLAKLIADVAPS AIRENDIKSYFGRKV AI DASMSIYQFLIAVRQ -GGDVLQNEEGETTS-LMGMFY MUSFEN1 . PRO	1 MGIKGLNNAI SEHVP S AIRKSDIKSFFGRKV AI DASMSL YQFLIAVRQQDGGQLTNEAGETTSHLMGMFY YST510 . PRO	1 MGVHSFWDIAG---PTARPVRLESLEDKRM AVDASIWIYQFLKA VRDQEGNAVKN-----SHITGFFR YSTRAD2 . PRO	1 MGVSGLWNILE---PVKRPV KLETLVNKRLA IDAS IWIYQFLKA VRDKEGNQLKS-----SHVVGFFR SPORAD13 . PRO	1 MGVQGLWKLLE---CSGROV SPEALEGKIL AVDISIWLQNQALKGVDRHGNSIEN-----PHLLTLFH HUMXPG . PRO	1 MGVQGLWKLLE---CSGHRV SPEALEGKVLA VDISIWLQNQALKGV RDSHGNV IEN-----AHLLTLFH MUSXPG . PRO	1 MGVQGLWKLLE---CSGRPINPG TLEGKIL AVDISIWLQNQAVKGARDRQGNAIQN-----AHLLTLFH XENXPG . PRO	1 MTINGIWENAHVV---RKVPINETMRDKT L SIDGH I WLYYESLKGCEAHHQQT-----PNSYLVFTFT CELRAD2 . PRO
80	90	100	110	120	130	140				
64 KTIHLLENDITPIWVFDGEPPK KEKTRVREMKE KAELKM KEAIKK -----EDFEAAKYAKRVSYLT P MJAFEN1 . PRO	64 RTINLMEAGIKPVYYVFDGEPP FEKKKE LEKR REARE EEAEK W REALEK-----GEIEEAR KYAQ RATRVNE PFUFEN1 . PRO	70 RTIRM MENGIKPVYYVFDGKPPQ Q KSGELAKRSERRAE A KQLQQA -----GAE0VE EKF TKRLV KVT K HUMFEN1 . PRO	69 RTIRM- ENGIKPVYYVFDGKPPQ Q KSGELAKRSERRAE A KQLQQA -----GMEEEVE EKF TKRLV KVT K MUSFEN1 . PRO	71 RTLMIDNGIKPCYYVFDGKPPDLK SHELTKRSSR VETEK KL A-----EA-----TTELEK MKQERRL V VSK YST510 . PRO	61 RICKLLYFGIRPV VFDGGVPV VLKRETIRQRKERR RGKRESAK STAR KL LAQ LQNGSNDNKR DS EVTM YSTRAD2 . PRO	61 RICKLLFFGIKPV VFDGGAPS KL RQTIQKRQARRLD RE ENATV T ANKLL Q MRHQAM LL KRD DA EV T Q SPORAD13 . PRO	61 RLCKLLFFRIRPI VFDGDAPL KK Q TL VKRRQR K DSASSRKT TE KL KK Q TL AKRRQR K DSASIDSRSRKT TE KL KK Q TL KRQAL KT DRI AA SVTG HUMXPG . PRO	61 RLCKLLFFRIRPI VFDGDAPL KK Q TL VKRRQR K DSASSRKT TE KL KK Q TL KRQAL KT DRI AA SVTG MUSXPG . PRO	61 RIQRLL ELKIIPIV V FONINASSAHE SKD QNEFVPRKRR S FGDSPFTNL V-----CELRAD2 . PRO	

FIG. 70A

150	KMVENCKYLLSLMGIPYVEAPSEGEAQASYMAKKGDVWAVVSQDYDALLYGAPRVRNLTITKEM-----	MJAFEN1 . PRO
150	MLIEDAKKLLELMGIPIVQAPSEGEAQAYMAAKGSVYASASQDDSLFGAPRLVRNLTTGKRKLPGK	PFFUFEN1 . PRO
150	QHNDECKHLLSLMGIPYLDAPSEAESAALVKAGKVYAAATEDMDCLTFCSPVLMRHLTASEAKKLPIQ	HUMFEN1 . PRO
156	QHNDECKHLLSLMGIPYLDAPSEAESAALAKAGKVYAAATEDMDCLTFCSPVLMRHLTASEAKKLPIQ	MUSFEN1 . PRO
134	EHNEEAQKLLGLMGIPYIIAPTEAEAQCAELAKGGKVYAAASEDMTLCYRTPFLRLTFSNEAKKEPIH	YST510 . PRO
134	DMIKEVQELLSRFGIPYITAPMEAQAQCAELLQLNLVDGIIITDDSDVFLFGGTICKIYKNMFHEKNY---VE	YSRAD2 . PRO
131	VMIKECQELLRLFGLPYIYAPOEEAQAQCSKLELKLVDGIVTDDSDDVFLFGGTTRVYRNMFNQNKF---VE	SPORAD13 . PRO
131	QMFLESQELLRLFGIPYIYAPOEEAQAQCAILDTDQTSGTITDDSDIWLFGARHVYRNFFNKNKF---VE	HUMXPG . PRO
131	QMFLESQELLRLFGVPYIYAPOEEAQAQCAVLDLSDQTSGTITDDSDIWLFGARHVYKNFFNKNKF---VE	MUSXPG . PRO
131	QMCLESQELLQLFGIPYIYAPOEEAQAQCAILDTDQTSGTITDDSDIWLFGARHVYKNFFSQNKH---VE	XENXPG . PRO
111	DHVYKTNALLTELGIKVIIAPGIDGEAQCARLEQLGVTSGCITTDFDYFLFGGKNLYRFDFTAGT-----	CELRAD2 . PRO
195	-----PELIELNEVLEDLRISLDDLIDIAIFMGTDYNPGGV--K--GIGFKRAYELVRSGVAK--DV	MJAFEN1 . PRO
200	NYYVE-IKPELILIEEVLKELKTREKLIELAILVGTDYNPGGI--K--GIGLKKALEIVRHSKDPLAKF	PFFUFEN1 . PRO
206	EFHLSRILQELGLNQEQQFVDLCLILLGSDYCESIRGPKRAVDLIIQK--HKSIIEIVRRLDPN----KY	HUMFEN1 . PRO
204	EFHLSRVLQELGLNQEQQFVDLCLILLGSDYCESIRGIGAKRAVDLIIQK--HKSIIEIVRRLDPS----KY	MUSFEN1 . PRO
204	EIDTELVLRLGLDLTIEQFVDLCLIMLGCDYCESIRGVGPVTALKLIKET--HGSIEKIVEFIESGESNNNTKW	YST510 . PRO
198	FYDAEISIKLLGLDRKNMIELAQLLGSDYTNGLKGMDYVSSIEVIAEF--GNLKNFKDWYNNNGDFDKRK	YSRAD2 . PRO
198	LYLMDDMKREFNVNQMDLIKLAHLLGSDYTMGLSRVGPVIALEILHEFPGDTGLFEKKWFQRLSTGHAS	SPORAD13 . PRO
198	YYQYYDFHNQLGLDRNKLINLAYLLGSDYTEGIPTVGCVTAAMEILNEFPGHGLEPLLKFS	HUMXPG . PRO
204	YYQYYDFYSQQLGLDRNKLINLAYLLGSDYTEGIPTVGCVTAAMEILNEFPGRGLDPLLLKFS	MUSXPG . PRO
119	YYQYADIHNOLGLDRSKLINLAYLLGSDYTEGIPTVGCVTAAMEILNEFPGQOGLEPLVLFKKEWSEAQKDK	XENXPG . PRO
198	175 SSTAACLHDIMHLSLGRMF-----	CELRAD2 . PRO

FIG. 70B

	290	300	310	320	330	340	350
251	LKKEVEYYDEIKRIFKEPKV-----				---TD--NYSLSLKLKDKEGIKFLVDENDFNYD	MJAFEN1.	PRO
265	QKQSDVDLHYAIKEFFLNPPV-----				---TD--NYNLVWRDPDEEGILKFLLCDEHDDFSEE	PFUFEN1.	PRO
269	PVPENWLHKEAHQLFLEPEV-----				---LDPESELKWSEPNNEEELIKFMCGEKQFSEE	HUMFEN1.	PRO
267	PVPENWLHKEAQQLFLEPEV-----				---VPDPESELKWSEPNNEEELVKFMCGEKQFSEE	MUSFEN1.	PRO
272	KIPEDWPYKQARMLFLDPEV-----				---IDGNEINLKWSPPKEKELEIYLCDDKKFSEE	YST510.	PRO
265	QETENKFEDLRKKLVNNEIIIDDDFPSVMVYDAYMRPEVDHDTTTPFVWGVPDLMRLRSFMKTQLGWPHE				YSTRAD2.	PRO	
268	KNDVNTPVKRINKLVGK-IIIPSEFPNPLVDEAYLHPAVDDSKQSFQWNGIPDLDLDELRQFLMATVGWSKQ				SPORAD13.	PRO	
268	KIRPNPNDTCKVKKKL--RTLQLTPGFPNPAVAEAAYLKPVVVDSKGSFLWKGPKDLDKIREFCQRYFGWNRT				HUMXPG.	PRO	
268	KVAENPYDTCKVKKKL--RKQLQTPGFPNPAVADAYLRRPVVDSRGSSFLWKGPKDUDKIREFCORYFGWNRM				MUSXPG.	PRO	
268	KMRPNPNDTCKVKKKL--RLLDLQQSFPNPAVASAYLKPVVVDESKSAFSWGRPDLEQIREFCESRFGWYRL				XENXPG.	PRO	
194	-----EKKVSRPHLISTAILLGCDYFORGVQNIIGIVSVFD-ILGEFGDDGNEEIDPHVILDRAFASYVRE				CELRAD2.	PRO	
	360	370	380	390	400	410	420
300	RVKKHVDKLYNLIA-----						MJAFEN1.
314	RVKNGLERLKKAI-----						PRO
320	RIRSGVKRLSKSRQGS-TQGRRDDFFKV-----						
318	RIRSGVKRLSKSRQGS-TQGRRDDFFKV-----						
323	RVKSGISRLKKGLKSG-IQGRLDGFF0VV-----						
335	KSDEILIPLIRDVNKRKK-----						
337	RTNEVLLPVIQDMHKKF-----						
336	KTDESILFPVLKQLDAQQQTQLRIDSFRLAQQKEKDAKRIKSQRQLNRAVTCLMRKEKEAASEIEAVSVAM						
336	KTDESILYPVLKHLNAHQQTQLRIDSFRLAQQKEKDAKLIKSHRLSRAVTCLMRKEKEAASEIEAVSVAM						
336	KTDEVLLPVLKQLNAQQQTQLRIDSFRLAQQKEHEAAG--LKSQRRLRAVTCLMKRKERDVEAEEVEAAVAM						
257	EIPARSEDTQRKLRLRRKKYNFPVGFPNCDAVHNAAITMYLRRPVSSEIPKIIPR-----AANFQQVAEIM						CELRAD2.
							PRO

FIG. 70C

430	440	450	460	470	480	490
314						MJAFEN1. PRO
327						PFUFEN1. PRO
348						GSL S HUMFEN1. PRO
346						GSL S MUSFEN1. PRO
351						PK-T YST510. PRO
357	KRINEFF					YSTRAD2. PRO
359	SNLTQFFEGNTNVYAPRVAYHFKSKRLENALSFKNQISNQSPMSEEIQAQADADFGESEKGSDDELORSRIL					SPORAD13. PRO
406	EKEFELDKAKRKTKQRGITNTLEESSSSLKRKRLDSKRKNTCGGFLGETCLSESSDGSSSEHAESSSLM					HUMXPG. PRO
406	EKEFELDDAKGKTOKREL PYK					MUSXPG. PRO
403	ERECTNQRKGQKTNTKS					XENXPG. PRO
322	MKECGWPATRTQKELALSIRRKVHLTTTVAQTRIPDFFAATKSKNFTPIVEPCESLEDYISANN					CELRAD2. PRO
500	510	520	530	540	550	560
314						-NKTKQQKTL MJAFEN1. PRO
327						-KSGKQSTL PFUFEN1. PRO
352	SAKRKEPEPKGST					KKKAKTGAAG HUMFEN1. PRO
350	SAKRKEPEPKGP A					KKKAKTGGAG MUSFEN1. PRO
354	KEQLAAAKRAQE					NKKLNKNKNK YST510. PRO
364						YSTRAD2. PRO
429	PREYISGDKKKLNITSKRISTATGKL					KKP SPORAD13. PRO
476	RRKKMMASKNSSDSSEDNFNLASLTPKTNSSISIENPRKTKLSTSL					HUMXPG. PRO
469	NVQRRTAAKEPKTSASDSONSVKEAPVKNGGATTSSSSDGGKEKMLVTARSVF GKKRRKLRARG					MUSXPG. PRO
458	SARQRSAEESKIGCSVDLVRDSPHQGRQGCVSTSSSDDEDGEDAKTVLVTARPVGKKRRKLSMK-					XENXPG. PRO
387	WMRKRKRSESPQILQHHAKRQVPDRK					RSVKIRAFKPYPPTDVI CELRAD2. PRO

FIG. 70D

DAWFKZ
322 DAWFKZ
335 ESWFKR
375 KFKRGK
373 KFRRGK
377 VTKGRR
390 --RKM
483 SKRRRK
546 RKRKTZ
538 RRKKKT
523 TVKRK
429 ELGDSD

MJAFEN1.PRO
PFUFEN1.PRO
HUMFEN1.PRO
MUSFEN1.PRO
YST510.PRO
YSTRAD2.PRO
SPORAD13.PRO
HUMXPG.PRO
MUSXPG.PRO
XENXPG.PRO
CELRAD2.PRO

FIG. 70E